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REVIEW ARTICLE

Isoniazid preventive therapy in correctional facilities: a systematic review

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SUMMARY

Tuberculosis (TB) remains a major cause of morbidity and mortality worldwide and the main cause of death in correctional facilities in middle- and low-income countries. Due to the closed environment and the concentration of individuals with TB-related risk factors, effective measures are required to control TB in such settings. Isoniazid preventive therapy (IPT) represents an effective and cost-effective measure. Despite international recommendations that IPT be integral to TB control, it is seldom deployed. A systematic review of interventions used to assess IPT initiation and completion in correctional facilities was conducted using published studies from two biomedical databases and relevant keywords. Additional references were reviewed, resulting in 18 eligible studies. Most (72%) studies were conducted in the United States and in jail settings (60%), with the main objective of improving completion rates inside the facility or after release. Studies that provided data about initiation and completion rates showed poor success in correctional facilities. Adverse consequences and treatment interruption ranged from 1% to 55% (median 5%) in reported studies; hepatotoxicity was the most prevalent adverse reaction. Despite its accelerating effect on the development of active TB, information on human immunodeficiency virus (HIV) status was provided in only half of the studies. Among the four studies where IPT effectiveness was assessed, the results mirror those described in community settings. Future studies require thorough assessments of IPT initiation and completion rates and adverse effects, particularly in low- and middle-income countries and where comorbid viral hepatitis may contribute significantly to outcomes, and in settings where TB and HIV are more endemic.

KEY WORDS: tuberculosis; prisons; jails; isoniazid; prevention

WITH NEARLY 2 billion people infected worldwide,[1] tuberculosis (TB) remains a major global public health problem, contributing significantly to morbidity and mortality. In 2009, the World Health Organization (WHO) estimated that there were 9.4 million incident TB cases globally. Nearly 85% of these cases were in the Asia and Africa regions and 11–13% of TB incident cases were co-infected with the human immunodeficiency virus (HIV). TB mortality that same year resulted in 1.68 million deaths.[2]

The problems associated with TB are magnified in correctional facilities. It is estimated that TB prevalence within correctional facilities is up to 100 times higher than in the general community.[3] Increased TB rates in correctional settings are attributable in large part to the high concentration of TB risk factors among incoming prisoners, including HIV infection, a history of substance use disorders, low socio-economic status, malnutrition, homelessness, previous containment in closed settings and inability to access community-based health care.[4,5] Additional contributing risk factors, such as poor ventilation, overcrowding and the recycling of individuals through the correctional setting, facilitate transmission of TB in these settings, including multidrug-resistant strains.[4,5] Staggering incarceration rates globally have resulted in more than 10 million people being imprisoned,[6] including 400 000 detained annually in compulsory drug detention centers.[7] These settings serve as important reservoirs of infection, resulting in TB transmission into the community after release and through prison staff.[3,8,9] Studies from the United States confirm this dynamic, demonstrating that approximately 40% of all persons diagnosed with TB disease annually in the United States had passed through a correctional facility.[10]

Although alternatives to incarceration are preferred, correctional settings do serve as potentially important and feasible settings for screening high-risk, difficult-to-access populations for active TB disease, latent TB infection (LTBI) and other infectious diseases.[11] From a public health perspective, these facilities are

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increasingly recognized as being important sites for TB prevention and control efforts.[12]

LTBI is one of the most prevalent infections among inmates in correctional facilities, including prisons, jails and detention centers.[13] Within long-term facilities or those that house a large proportion of individuals with HIV infection, LTBI may have sufficient time to progress into active TB disease (with a 10% lifetime risk for immunocompetent subjects compared to a 10% annual risk for HIV-infected persons[14]), with resultant transmission to other inmates and staff.[13,14] In prisons where many prisoners are malnourished, the lifetime risk of progressing to TB disease is even higher.[3]

Prevention of active TB among those with LTBI is effective, safe and inexpensive. Isoniazid preventive treatment (IPT), confirmed in two meta-analyses, is effective at preventing progression to active TB disease in 60% of non-HIV-infected and 36% of HIV-infected populations.[15,16] Recent WHO guidance for resource-constrained settings recommends that IPT be administered to all HIV-infected persons, irrespective of tuberculin skin test (TST) reactivity;[17] however, clinical trials suggests that it is more effective among those with positive TST results.[15,16]

Although isoniazid (INH) is well-tolerated, drug-related hepatotoxicity occurs in 1–2% of cases. The frequency of hepatotoxicity is negligible among those aged ⩽35 years, and increases with age, alcohol consumption and among Asian men. Analyses of IPT studies confirm that benefits outweigh the risks, even among elderly persons,[18,19] and have resulted in recommendations to offer IPT to all persons with positive TST, irrespective of age.[20]

Despite these general recommendations and the unique characteristics and dynamics of correctional inmates compared to those in community settings, IPT is seldom provided in closed settings (prisons, jails and detention centers). Reasons for the lack of implementation of IPT have included concerns about lack of effectiveness, adherence, safety and cost of IPT in these settings. To address these stated reasons, we conducted a systematic literature review to explore published studies that were applicable to correctional facility inmates to address issues related to the initiation and completion of IPT either within these settings or after release, to provide empiric guidance for public policy and provide insight into future research studies.

METHODS

Literature search

A systematic review of the literature was conducted using PubMed and Web of Science following PRISMA guidelines.[21,22] Key words included 'correctional', 'prison', 'jail', 'detention' and 'isoniazid' or 'isoniazid preventive therapy'. Articles were included if published from 1966 to January 2011 and written in any language. Additional primary references from review articles and international reports were also reviewed to ensure completeness. The three non-English articles that were written in Spanish were translated using Google Translate; one author (FLA) is fluent in Spanish.

Exclusion criteria

Articles involving studies of IPT that were not conducted within correctional facilities, that used regimens other than INH or were not clinical research studies (i.e., editorials, letters of correspondence, author's reply and guidelines) were excluded from the review.

Data extraction

Eligible studies were reviewed independently by two authors (HAAA, FLA). Due to heterogeneity in study reporting, a structured data extraction form was created that included each of the following: 1) exact site and continent where the study was conducted; 2) year of publication (categorized by decade); 3) study setting where the study was conducted (whether prison, jail or both); 4) study design (categorized as cross-sectional, cohort, case-control, or randomized controlled trial [RCT]); 5) study outcome of interest (whether the objective of the study was to examine IPT completion within the facility or after release, impact on TB incidence or IPT safety); 6) whether or not HIV infection rates were described; and 7) participants' socio-demographic characteristics.

In relation to the outcome of interest, extracted data were extended to include relevant information on enrollment prevalence (prevalence of inmates diagnosed with LTBI and/or started IPT), prevalence of active TB prior to starting IPT, prevalence of hepatitis C virus (HCV) co-infection, history of alcohol use prior to incarceration, liver disease among participants, duration and completion rates of IPT, reasons for defaulting, prevalence and types of adverse effects (particularly that of drug-induced hepatitis) and preventive efficacy of the intervention (difference in TB development at the end of the follow-up period).

Data analysis

Extracted data were entered into a Microsoft Excel spreadsheet (Microsoft, Redwoods, WA, USA) for final analysis through SPSS® version 17.0 (Statistical Package for the Social Sciences Inc, Chicago, IL, USA). Results were expressed as percentages. Descriptive statistics (mean and median) were described when data could be pooled.

RESULTS

Search strategy

The search strategy initially yielded 43 unduplicated studies (Figure); 16 were subsequently excluded

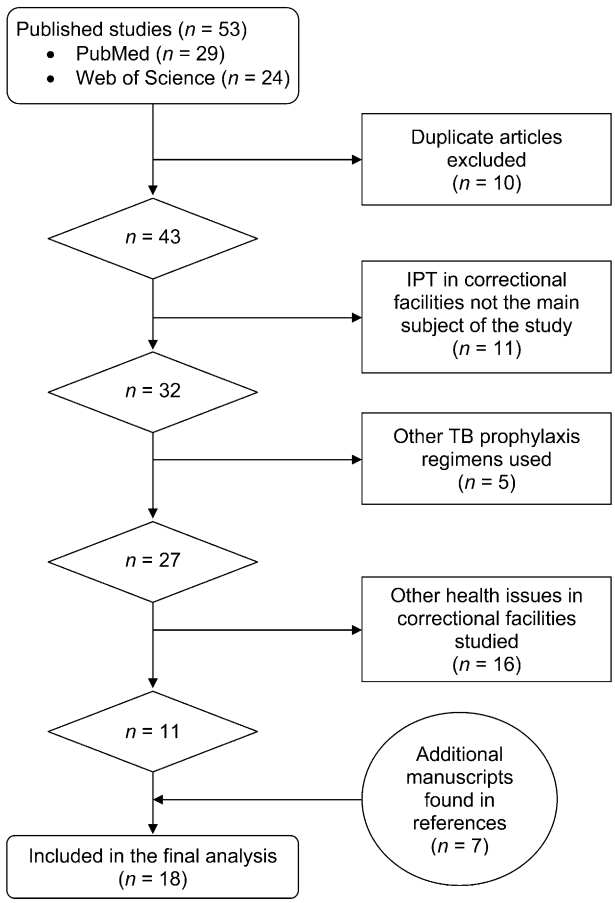

Figure Process of search and inclusion in the final analysis. IPT = isoniazid preventive therapy; TB = tuberculosis.

because they did not involve IPT (e.g., multidrug resistance in prisons, post-release general health care to inmates and TB outbreak investigation in prison), and another 11 were excluded because they did not involve IPT within the correctional setting or addressed INH resistance. Five more articles were excluded because regimens other than INH were examined. As a result, 11 published studies remained from the initial search and an additional seven studies were obtained after secondary review of references, resulting in 18 eligible papers for final assessment.[10,12,19,23–37] The details of the 18 eligible studies are provided in the Table.

Year of publication

The majority (n = 12, 67%) of the studies were published after 2000, five were published between 1990 and 1999 and one in 1989.

Geography

The prevalence of TB differs among regions and countries. In general, TB prevalence is highest in sub-Saharan Africa and South-East Asia and lowest in Europe and North America. Most of the studies (n = 13, 72%), however, were conducted in North American correctional settings, all in the United States. Four studies were conducted in Europe—all in Spain, and only one study was from Singapore, a country not highly representative of Asia's TB epidemic.

Study setting

Most studies (n = 11, 61%) were conducted solely in jail settings, while two additional studies were conducted in both jail and prison settings and five were conducted in prisons.

Study design

More than half of the studies (n = 10) were prospective cohort studies, while the remainder were either cross-sectional (n = 5) or RCTs (n = 3).

Primary outcome of the study

Nearly all of the studies (n = 15, 83%) examined IPT completion rates among inmates and interventions to improve them. Completion of IPT in jail (n = 4) or after release from jail (n = 7) was the primary objective among the reviewed studies. Two additional studies examined IPT completion rates in facilities that combined both jail and prison, while two were conducted solely among prison detainees. Two studies explored the impact of IPT on TB incidence inside prisons, and one was conducted to compare the effectiveness and completion rate of IPT using a brief, non-standard TB prophylaxis regimen using rifampicin (RMP) plus INH for 3 months.

Demographic characteristics of participants

The age of the participants varied among the studies. In half of the studies, the mean age of participants was 30–39 years, while four studies had younger study populations, with mean age 20–29 years. An additional study included participants aged <40 years, while age was not mentioned in two studies. Over 90% of study participants were men.

HIV prevalence inside the facility

Voluntary counseling and HIV testing (VCT) was available in most of the correctional facilities where the studies were conducted. Information on HIV prevalence among participants (or in the facility) was not provided in half of the studies, while the remaining nine studies showed variable HIV prevalence, ranging from a high of 30% in Spain to diverse prevalence elsewhere, including in the United States, where there were low VCT rates. The study from Asia provided no information about HIV.

Prevalence of TB inside the facility (pre-intervention)

More than 60% (n = 11) of the articles did not provide information about the prevalence of active TB in the correctional setting before the start of the study. The remaining seven studies showed varying prevalence of active TB disease in the setting, even within

Table Summary of INH preventive therapy in correctional facilities

Author, year, country, reference	Study design	Study setting (sample size)	Sex, mean age, race/ethnicity	Study objective(s)	HIV prevalence	Completion rate	Adverse reaction (reaction due to hepatotoxicity)
Lincoln, 2004, USA[26]	Cross-sectional	Jail (146)	Male (93%), <40 years (82%)	Completion in jail	Not reported	74%	14% (90%)
Bandyopadhyay, 2002, USA[24]	Cross-sectional	Jail (168)	Male (90%), 35 years	Completion after release	Not reported	55%	Not reported
MacIntyre, 1997, USA[19]	Cohort	Prison (358)	Male (95%), 33 years, Black (70%)	Impact on development of TB	9% of the prison (only 36% tested)	Not reported	Not reported
White, 2002, USA[34]	RCT (education; incentive; usual care)	Jail (558)	Male (90%), 29 years, Hispanic (53%)	Completion after release	Not reported	23%/12%/12%	1%
White, 1998, USA[37]	RCT (incentive+ TB education; TB education alone)	Jail (79)	Male (98%), 32 years, Hispanic (50%)	Completion after release	Not reported	6%	Not reported
Tulsky, 1998, USA[33]	Cohort	Jail (151)	Male, 26.5 years, Hispanic (36%)	Completion after release	Not reported	3%	Not reported
Nolan, 1997, USA[30]	Cohort	Jail (483)	Male (92%), <35 years (62.5%), Hispanic (26%)	Completion after release	1.1% (of the facility)	60%	1%
Alcabes, 1989 USA[23]	Cohort	Jail (74)	Male, <19 years (44%), Black	Completion in jail	Not reported	37.5%	Not reported
Martinez Alfaro, 2000, Spain[29]	RCT (INH+RMP; INH alone)	Prison (133)	Male, 31 years	Comparison to 3 months RMP+INH efficacy	All recruits	57%	51% (41%)
Romero Saldana, 1997, Spain[32]	Cohort	Prison (52)	Male (76%), 29.6 years	Completion in prison	32.7% (of the cohort)	44.23%	Not reported
White, 2005, USA[36]	Cohort	Jail (527)	Male (91%), 30 years, Hispanic (61.8%)	Completion in jail + efficacy	Not reported	31.6%	6.8% (58%)
Lobato, 2003, USA[12]	Cohort	Jail and prison (21479)	Male (90%), 30 years, non-White (74%)	Completion in prison or jail	14.5% (of facility–16% tested)	55.9%	2.9% (44.2%)
Martin, 2001, Spain[28]	Cohort	Jail and prison (632)	Male (93%), 29 years, White (85%)	Impact on TB incidence	15% (of the cohort)	Not reported	Not reported
Chee, 2005, Singapore[25]	Cohort	Jail and prison (455)	Male (90%), age not reported, Malay (52%)	Efficacy and completion in facilities	Not reported	87%	4.8% (90%)
White, 2005, USA[35]	Cohort	Jail (268)	Male (91%), 30 years, Hispanic (61%)	Completion after release	Not reported	39%	5%
Hayden, 2004, USA[10]	Cross-sectional	Jail (1)	Male (95%), 36 years, non-White (85%)	Enrolment and completion in jail	1.1% (of the cohort)	1 (100%)	Not reported
Reichard, 2003, USA[31]	Cross-sectional	Jail (313)	Not reported	Completion after release	2.7%	20.7%	Not reported
Martin, 2000, Spain[27]	Cross-sectional	Prison (84)	Male (93%), 32 years	Completion in prison	10.5%	46.4%	26% (4%)

INH = isoniazid; HIV = human immunodeficiency virus; RCT = randomized controlled trial; TB = tuberculosis; RMP = rifampin.

the same country (United States, as an example). The prevalence of active TB within the setting was highest in the study from Singapore (1.1%), and varied in the United States from 6.8 to 105 per 100 000 inmates.

Enrollment and completion rates

Latent TB infection

Only half of the studies provided information on the prevalence of LTBI among inmates. Prevalence varied even among inmates within the same country. Generally, prevalence in US correctional facilities was less than 30% of tested inmates, while studies from Spain showed nearly 50% prevalence. In the Singapore prison, nearly 70% of inmates had LTBI.

Rate of prisoners starting IPT

Inside correctional facilities, many factors might deter eligible inmates from being initiated on an LTBI treatment course. Fourteen studies (77%) presented data about the rate of enrollment of inmates with LTBI. Median enrollment was 57% (range 5–93) among the 14 studies that presented such data. Reasons for low enrollment included transfer to another facility or a short sentencing period in five studies; participant refusal in three studies; age >35 years in one study; and previous IPT course in one study. No reason was provided in the four remaining studies.

Duration of IPT

Trials of the duration of effective IPT in the general community have been conducted for 6-, 9- and 12-month IPT courses. Of the 18 correctional studies, eight (44%) used the 1994 Centers for Disease Control and Prevention (CDC) recommendation of IPT for 6 months in HIV-negative and 12 months for HIV-infected persons,[38] although three of these were conducted after publication of the 2000 joint American Thoracic Society (ATS) and CDC recommendations.[20] Six studies used 6-month IPT, regardless of HIV status and four studies used 9-month IPT.[20]

Completion rate

Nearly all of the studies (89%) provided data on IPT completion rate, irrespective of whether the treatment was within the facility or given after release (particularly for short-term facilities such as jails). Median completion rate was 44%, ranging from 3% to 87% for the 16 studies in which data were available. One study was excluded from the rate analysis as only one participant was enrolled in the study and he completed treatment inside the facility. Reasons for non-completion were transfer or release from the facility ($n = 5$), loss to follow-up ($n = 7$), refusal to complete IPT ($n = 6$), and adverse reactions that required discontinuation of IPT ($n = 9$). Reported adverse reactions were variable, and ranged from 1% to 55%. Although treatment cessation was low overall, hepatotoxicity was the most commonly reported adverse reaction leading to treatment cessation or interruption. In the one study in which mortality was reported, four of 64 participants died (mortality 6.25%); none of the deaths were related to IPT and all were HIV-infected. Two of the studies provided information on HCV co-infection; prevalence was 21% among a US cohort and 71% among Spanish participants. Hepatotoxicity requiring treatment cessation was reported in respectively 12.5% and 22.5% of participants in these two studies.[26,29]

Effectiveness

Four (22%) studies provided data on TB incidence during the designated follow-up period. TB incidence did not differ (4.23 vs. 2.08 cases per 100 person-years [py]; adjusted odds ratio [aOR] 0.5, 95% confidence interval [CI] 0.09–2.8) in a study in Spain comparing the efficacy of 12 months of INH with 3 months of INH+RMP after a 19-month follow-up period. Another Spanish study showed that TB incidence was significantly higher (17 vs. 1 case per 100 py) among those who were not given IPT than among those who completed ⩾6 months of IPT. An observational US jail study reported no TB cases among 176 inmates who completed a full 6-month course of IPT after 5 years of follow-up. Active TB did develop in three cases, however, resulting in an annual rate of 108 cases per 100 000 population among those who initiated but did not complete IPT. Finally, the study from Singapore reported the development of four TB cases, all of whom were direct contacts of an active TB case and who had not started IPT due either to elevated hepatic transaminases or to TST-negative status.

DISCUSSION

Despite the increased contribution of TB in criminal justice settings, there are few data on the utility and implementation of IPT. It should, however, be noted that there appears to be increasing interest in this issue, as most of the data are reported from the past decade. Unfortunately, the majority of the studies were conducted in low TB endemic, high-income countries (72% of the studies were conducted in the United States). This divergence between where IPT studies were conducted and where there is the greatest need geographically may, in part, reflect the WHO recommendation to focus on increased detection and early diagnosis in low- and middle-income prison settings, where resources are often constrained.[3] The wisdom of such an approach may, however, be short-sighted, as these settings, particularly prisons, are highly structured, can ensure adherence to therapy (especially in long-term facilities) and shoulder a disproportionate burden of disease, including both HIV and TB. Data collected since 2000 may, in addition, need reconsideration, as the prevalence of HIV in these settings appears to have been increasing

over the past decade since the recommendations were made.[6,39]

Jails, or short-term detention facilities, may be less than ideal for routine implementation of IPT unless inmates have at least 9 months remaining on their sentence. They are, however, important sites not only for identifying individuals at increased risk for infectious diseases, including IPT-eligible persons, but also for initiating and continually engaging individuals from the community who are already on treatment.[11] Most reported TB outbreaks occurred in prisons, reinforcing the importance of IPT in longer-term facilities.[40] In addition, periods of incarceration inside preadjudication facilities (e.g., jails, pre-trial detention, etc.) are usually unpredictable, as most detainees leave within a relatively short time period and a detainee's status changes frequently.[11] Short incarceration periods in such facilities might represent a challenge for IPT implementation in terms of enrollment and completion rates, although data are emerging for the creation of interventions that effectively link treatment from the criminal justice system with communities.[11,41] In the present review, 11 of 18 studies were conducted in jails, and all sought to improve IPT completion during incarceration and/or facilitate it after release. In four studies from the United States, although completion rates were low (30%, 33% and 39%) during jail detention, they were even lower (17%) when patients were followed up after release. As there is considerable overlap between individuals with TB and substance use disorders,[42] emerging data suggest that treatment outcomes of infectious diseases after release are optimized when the substance use disorder is treated simultaneously, including the use of medication-assisted therapies.[43,44]

Post-release interventions to improve IPT completion have had variable results, but are somewhat disappointing. Tulsky et al. reported that simple prerelease education and counseling was associated with a low (3%) linkage to the first visit to a TB clinic within 1 month of release.[33] White et al. demonstrated that a single educational session delivered immediately prior to release from jail did not improve IPT completion (52% vs. 50% for controls),[35] while other RCTs found that more intensive educational group sessions had relatively poor outcomes, but significantly increased (by two-fold) jail post-release IPT completion compared to controls (23% vs. 12%).[34,36,37] Overall, completion rates were relatively low, but the added contribution of a financial incentive did not appreciably improve IPT completion compared to controls (12% vs. 12%).

To address these dismal outcomes, studies were conducted to examine the impact of a short, but recognized LTBI treatment regimen (2 months of RMP+pyrazinamide, 2RZ) on completion rates within jail settings. Lincoln et al. found that compared to 6 or 12 months of IPT, short-course treatment was significantly more successful in completing LTBI prophylaxis (88% vs. 74%) and was equally well-tolerated.[26] In another prospective US jail study, the 2RZ regimen was well-tolerated and, compared to standard IPT, resulted in a four-fold increase in the numbers of inmates who completed LTBI treatment. Tolerability was high, with only 8% of participants discontinuing treatment due to adverse side effects.[45]

Another study that included jail inmates and homeless persons in three US cities examined adverse events and treatment completion rates using the 2RZ treatment regimen. Completion rates of respectively 47.5% and 43.6% among jail inmates and homeless persons were reported, suggesting that medically marginalized individuals in jails were equally likely (or unlikely) to complete the regimen, and that jail detention per se did not adversely affect completion rates. Overall, 13.4% of subjects who discontinued their treatment did so due to adverse effects. Hepatotoxicity was the cause of drug cessation in 6% of the participants, and there was one death due to liver failure. Increasing age, abnormal baseline aspartate aminotransferase (AST) levels and unemployment within the past 24 months were independent risk factors for hepatotoxicity.[46]

In 2002, the US-based CDC amended their LTBI treatment guidelines as a result of increased safety concerns about the short-course 2RZ regimen after a series of fatalities. The new guidance preferred the 9-month IPT regimen, and recommended that the 2RZ regimen should be used with caution, and only in those without underlying liver disease or previous INH-related liver injury. Moreover, subjects prescribed the 2RZ regimen should have hepatic transaminases and bilirubin measured bimonthly,[47] which may not be feasible in prisons and resource-constrained countries.

Data from an RCT of over 8000 subjects recently confirmed that combined INH+rifapentine, administered once weekly for 12 weeks, resulted in significantly fewer cases of active TB observed over a 33-month observation period (7 vs. 15), higher completion rates (82% vs. 69%), and a similar safety profile compared to standard 9-month IPT.[48] This approach has considerable promise for treatment in short-term criminal justice settings, but has yet to be empirically tested, especially in populations with high rates of viral hepatitis,[49,50] where toxicity levels may be increased.

Finally, Nolan et al. investigated the impact of instituting an outreach program to improve inmates' adherence after release from jail.[30] IPT was provided as 900 mg twice weekly under direct observation (directly observed therapy) by an outreach worker. Despite the less frequent dosing, IPT completion rates were low (60%), albeit higher than all other studies reported, with an estimated modest number of TB cases prevented (4.4 future TB cases). As a result, they recommended that resources might be better directed

towards screening and treatment of active TB inside jails. A post-release cost-effectiveness analysis followed this study arguing against avoiding IPT in jails. Despite the low completion rate (55%), TB screening and IPT treatment in jail with follow-up after release was cost-effective (programmatic cost = US$32 866) compared to the public health cost due to TB reactivation (US$42 093), particularly for motivated inmates.

The CDC subsequently set national benchmarks for effective IPT programs in US correctional facilities. Standards include screening of all inmates for TB disease and LTBI, initiating IPT in at least 80% of inmates with LTBI, and completion rates of LTBI of at least 75%.[12] Despite that, adherence to these recommendations remains low. In this review, the median IPT enrollment rate of inmates diagnosed with LTBI was 57% and only two studies reported achieving the 80% enrollment benchmark. Reasons cited for low enrollment rates were transfer between or release from a correctional facility, refusal, age limit (following the previous CDC recommendations) and previous course of IPT. Median IPT completion rates (44%), however, were even more dismal, and only one cited a completion rate exceeding the recommended 75%.

Community-based IPT enrollment and completion rates are similarly low. A multisite prospective cohort of HIV-infected patients from 28 Italian specialty hospitals resulted in as few as 39% of eligible subjects initiating IPT. Physician factors (mostly due to fear of adverse reactions), medical contra-indications and subject refusal were cited as the main reasons for low enrollment. Although 72% of those initiating IPT completed it, more than half of non-completers self-discontinued their medication, while the rest did so due to adverse reactions (neuropathy and elevated AST levels).[51] A retrospective assessment of IPT from a TB clinic in Rhode Island confirmed that 81.6% of patients initiated IPT, but only 61.7% completed the 9-month course. The high initiation rate in this setting may be due to the increased intrinsic motivation of individuals who followed through on a referral to receive services from a specialty TB clinic. The lower retention on IPT, however, was due to loss to poor follow-up (35.7%), adverse effects (2.6%), pregnancy, transfer to another state and death unrelated to IPT.[52] In recognizing the high default rate from IPT, Chaisson et al. conducted an RCT to identify the optimal adherence strategy for completing IPT among injecting drug users.[53] Subjects either received directly observed preventive therapy (DOPT) twice-weekly, self-administered therapy with peer education and counseling, or routine standard of care. Each group was re-randomized to receive a monthly US$10 stipend for optimal adherence. Although adherence was highest in the DOPT groups, IPT completion was similar for all groups, and financial incentives did not improve either adherence or completion rates. Reasons for non-completion include failure to return (12.3%), voluntary withdrawal (1.3%), death unrelated to IPT (1.6%), adverse reactions (0.6%) and development of active TB (0.6%).

Adverse reactions to IPT contribute significantly to treatment non-completion, including death. INH-induced hepatotoxicity, defined as hepatic transaminases exceeding five times the upper limits of normal, is considered one of the most common and serious adverse consequences of IPT. Risks associated with this complication include increasing age, Asian race, female sex, alcohol consumption, liver disease (particularly viral hepatitis) and elevated baseline hepatic transaminases. The ATS recommends frequent monitoring of liver enzymes among those who chronically consume alcohol, take concomitant hepatotoxic medications, have viral hepatitis or other pre-existing liver disease or abnormal baseline alanine aminotransferase, and in pregnant women.[20] In this review, adverse events were responsible for treatment cessation in a median of 5% of individuals, with hepatotoxicity being responsible for half of these. The one study that compared hepatotoxicity within a correctional facility with that of the general community was in Singapore, where this adverse effect was 10 times higher among correctional inmates (4.8% vs. 0.45%);[25] one explanation is that IPT is supervised within structured correctional settings, resulting in higher drug exposure due to improved adherence. Alternatively, the prevalence of viral hepatitis co-infection may have been higher among prisoners due to mandatory incarceration of drug users in many international settings. Two studies further examined the increased risk related to INH-related hepatotoxicity, including two confirming HCV infection, four confirming alcohol consumption and one study reporting underlying liver disease (etiology not specified).[26]

HIV-infected patients remain the highest priority for screening and initiating treatment for LTBI.[54] At the time of these studies, the WHO[3] and CDC[20] recommended IPT for all HIV-infected inmates with a positive TST ($\geqslant$5 mm), regardless of age. In this review, however, only half of the studies reported information regarding HIV infection within the facility or among subjects participating in the studies. New international guidelines now recommend that IPT be provided for all HIV-infected persons, irrespective of TST reaction or previous TB status.[17] There are no data, however, to support the efficacy, completion rates or adverse consequences of this approach in correctional settings in low- and middle-income countries.

Although IPT's effectiveness in preventing active TB has been documented in many geographically diverse global settings,[15,16,26] only four studies reviewed here reported reductions in TB incidence after treatment. Findings from within correctional facilities mirror results from the general community, i.e., IPT effectively reduces progression from LTBI to active TB disease among incarcerated people.

CONCLUSION AND RECOMMENDATIONS

Despite several decades of IPT use, assessment of its use in correctional facilities remains limited, yet continues to highlight the importance of correctional settings being ideal sentinel sites for screening and treatment of active and LTBI. The review revealed a paucity of studies addressing IPT implementation in correctional facilities, necessitating further exploration of the efficacy and safety of IPT in closed settings. Most of the studies of LTBI treatment have primarily been conducted in high-income countries, particularly where TB prevalence is low. In general, initiation and completion rates of IPT remain low, particularly in jails and short-term detention centers, and innovative strategies are urgently needed to provide evidence for more effective approaches to ensure treatment initiation and retention.

Although the review affirmed the safety of IPT among inmates, it has not been sufficiently studied in settings where the syndemic of HIV, TB and injection drug use converge within correctional settings, where IPT may cause greater adverse side effects due to the additive hepatotoxicity or peripheral neuropathy from concomitant prescription of antiretroviral medications and/or the potential increase in hepatotoxicity among those co-infected with viral hepatitis.[42] Furthermore, the efficacy of IPT in correctional facilities needs to be investigated further, particularly in high-burden countries, where TB transmission remains unacceptably high in these settings.

Although seemingly daunting, it remains of paramount public health importance to control TB within correctional settings as it will have a dramatic impact on community levels of TB. This is particularly relevant, as nearly all prisoners with LTBI return to their communities and thereby contribute to growing community TB epidemics, including those involving multidrug-resistant and extensively drug-resistant strains.

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RÉSUMÉ

Au niveau mondial, la tuberculose (TB) reste une cause majeure de morbidité et de mortalité et constitue la principale cause de décès dans les prisons des pays à revenus moyens ou faibles. Des mesures efficientes s'imposent pour lutter contre la TB dans de tels contextes en raison des environnements renfermés et de la concentration des individus porteurs de facteurs de risque liés à la TB. Le traitement préventif à l'isoniazide (IPT) représente une mesure efficiente et d'un bon rapport coût-efficacité. En dépit des recommandations internationales qui considèrent que l'IPT fait partie intégrante de la lutte contre la TB, celui-ci est rarement pratiqué. Une revue systématique des interventions utilisées pour évaluer la mise en route et l'achèvement de l'IPT dans les prisons a été menée sur base des études publiées dans deux bases de données biomédicales et avec les mots-clés correspondants. Des références complémentaires ont été revues, ce qui a mené à 18 études éligibles. La plupart des études (72%) ont été menées aux Etats-Unis et dans les contextes de prisons (60%), avec comme objectif principal l'amélioration des taux d'achèvement à l'intérieur de la prison et après libération. Les études ayant fourni des données concernant les taux de mise en route et d'achèvement n'ont montré que des succès médiocres dans les services correctionnels. Les effets indésirables ainsi que l'interruption du traitement évoluent entre 1% et 55% (valeur médiane 5%) dans les études où ils sont signalés, et l'hépatotoxicité constitue la réaction indésirable la plus prévalente. En dépit de l'accélération du développement d'une TB active due au virus de l'immunodéficience humaine (VIH), l'information sur le VIH n'apparaît que dans la moitié seulement des études. Dans les quatre études où l'efficience de l'IPT a été évaluée, les résultats sont le miroir de ceux décrits dans les contextes de la collectivité. Des études ultérieures exigent une évaluation approfondie des taux de mise en route et d'achèvement de l'IPT et de ses conséquences défavorables, particulièrement dans les pays à revenus faibles ou moyens et où l'hépatite virale peut contribuer de manière significative comme co-morbidité aux résultats ainsi que dans les contextes où la TB et le VIH sont plus prévalents.

RESUMEN

La tuberculosis (TB) sigue siendo una causa importante de morbilidad y mortalidad en el mundo y la principal causa de muerte en los establecimientos penitenciarios de los países de medianos y bajos recursos. En estos ambientes confinados que albergan una concentración de personas con factores de riesgo de padecer la TB, se precisan medidas eficaces de control de la enfermedad. El tratamiento preventivo con isoniazida (IPT) constituye una medida eficaz y rentable. Pese a las recomendaciones internacionales, rara vez se suministra este tratamiento preventivo. Se llevó a cabo un análisis sistemático de todas las intervenciones utilizadas con el fin de evaluar la iniciación y la compleción del IPT en los establecimientos penitenciarios, a partir de dos bases de datos biomédicas, utilizando palabras clave pertinentes. Se analizaron otras referencias y se incluyeron 18 estudios idóneos. La mayoría de los estudios (72%) tuvo lugar en los Estados Unidos en centros de reclusión (60%) y su principal objetivo era mejorar las tasas de compleción del tratamiento dentro del establecimiento y después de la liberación. En los estudios que aportaban datos sobre las tasas de iniciación y de compleción del tratamiento se observaron bajos índices de éxito terapéutico en los centros correccionales. Las reacciones adversas y la interrupción del tratamiento comunicados en los estudios oscilaron entre 1% y 55% (mediana de 5%) y el efecto adverso más frecuente fue la hepatotoxicidad. Aunque la coinfección por el virus de la inmunodeficiencia humana (VIH) es un factor que acelera la evolución hacia la enfermedad tuberculosa activa, solo la mitad de los estudios suministraban información al respecto. Los resultados de los cuatro estudios en los cuales se evaluó la eficacia del IPT fueron equivalentes a los descritos en los entornos comunitarios. En los estudios futuros, es preciso realizar una evaluación completa de las tasas de iniciación y de compleción del IPT y de sus reacciones adversas, sobre todo en los países de medianos y bajos ingresos donde la coinfección por el virus de la hepatitis puede influir en forma considerable en los desenlaces y en los entornos donde la TB y la infección por el VIH son más endémicas.